On clustering

Older people are often a delight, sometimes frustrating. There are lots of them about, and there will be more before long, and at some time they will include us. So it is perhaps time to think about them and their problems a little more. For professionals helping with their health problems, a little extra light and evidence would probably help as well.

Although the medical care of older people is similar to that of younger age groups, we have surprisingly limited knowledge even of what is normal in the elderly. Clinical trials of treatments rarely include older patients and trials specific to older patients are uncommon. Diagnosis and treatment for this very important group of people depends largely on informed guess work based on evidence from younger patients, plus some dollops of experience and intuition.

While younger people in good or ill health are often broadly similar, there is more of a spectrum in older people, and fit 90 year olds are not the same as sick 70 year olds. Perhaps there is a tendency to cluster. Bandolier was taken by a description of a typical patient in an arthritis clinic: older woman, significantly overweight, trapped in a negative pattern of continual weight gains and pain, accompanied in turn by decreasing activity and functional capacity.

Hands up anyone who is average

Bandolier 95 highlighted the propensity of some people in trials to do well, and some to do not so well. Yet often we are given average results where few if anyone is average. Perhaps trials are being reported better, but this clustering into good or not good responders is something seen more often. It is a challenge to trialists, and especially to folks doing meta-analyses, if the average values they do sums with don't actually mean very much. Bandolier will return to clustering in more detail in future. In the meantime we would welcome any thoughts, insights, or key references that you know of that we have missed.

In this issue

CHOLESTEROL IN OLDER PEOPLE

One of the most frequently asked questions of Bandolier is about cholesterol in the elderly, and the role of statins in older people (over 70s for convenience), and particularly in the oldest old (over 80s). As best Bandolier knows, there is no simple answer, but there have been a number of studies in recent years, all cohort studies.

There is a general link between low serum cholesterol and increased mortality, though cardiovascular disease remains the highest cause of death. Of course, in older people there are many confounding factors, particularly the propensity for increasing numbers of medical conditions, and be taking increasing numbers of drugs. Both factors tend to increase with age, while kidneys, liver, lungs, heart and muscle have reducing efficiency. Older people tend to eat less, as well.

Bandolier has chosen to review briefly six large studies (at least 1,000 people) published in the last four years. The hope is that by pulling some common threads together we have a more integrated view, if still imperfect understanding.

Honolulu [1]

This was part of a large epidemiological study starting in 1965 with 8,000 Japanese/American men born between 1900 and 1919. The study was based on examinations in 1991-1993, with mortality to end 1996. The examination consisted of demographics, function tests, blood tests, and ECG.

Results

There were 3,572 men aged 71-93 years. Mean serum cholesterol fell from 5.0 mmol/L in those aged 71-74, to 4.6 in those older than 85 years. Analysis by quartiles of serum cholesterol showed that age-adjusted mortality was highest in the quartile with the lowest serum cholesterol (Figure 1).

Figure 1: Mortality and cholesterol levels
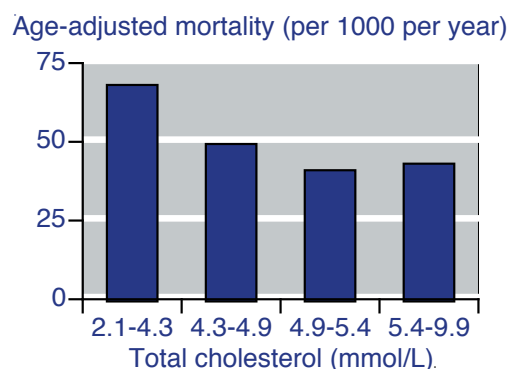
Figure 2: Cholesterol and weight loss or poor physical functioning
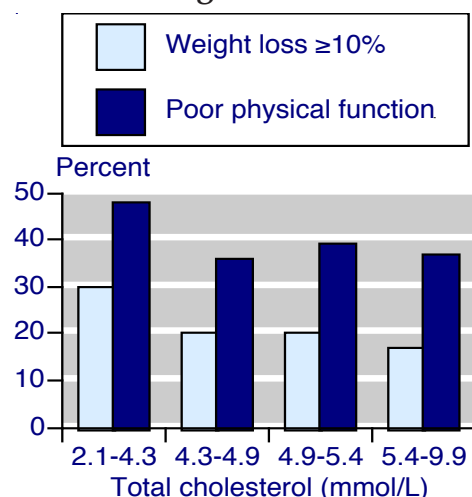
Men in the lowest quartile for total cholesterol were more likely to have a history of weight loss and poor physical functioning (Figure 2). Much of the statistical relationship between low cholesterol and increased mortality was lost when risk factors and frailty measures were taken into account, but it remained in men who had low total cholesterol for about 20 years.

Italy [2]

In 1985 3,282 Italians aged 65 years or older were screened, with demographic data, blood samples, and other cardiovascular and respiratory measurements made. Subsequent mortality was assessed annually by monitoring discharge records and death certificates.

Results

There were slightly more women than men, the mean age was 74 years and the mean total cholesterol 5.7 mmol/L. The average BMI was 26, and 61% were classified as overweight. More men smoked, and more women had diabetes diagnosed. Total follow up was 12 years, with 1,599 deaths.

For women, but not men, overall mortality was significantly higher in those with the lowest cholesterol (below 5.1 mmol/L). Both men and women in the lowest quartile of cholesterol (below 5.1 for women and 4.7 for men) had increased mortality compared with participants with higher cholesterol and BMI above 25.

Women and men in the lowest quintile of cholesterol had higher rates of death from cancer or other causes than those in the highest quintile. For men but not women, the highest quintile of cholesterol conferred an increased risk of coronary heart disease death.

Italy [3]

The study population was all patients aged 65 years or older admitted to 35 clinical centres (geriatric and internal medicine wards) in Italy during May-June and September-October 1995 with data on demography, diagnosis, and blood and other analyses.

Figure 3: Cholesterol and weight loss or poor physical functioning
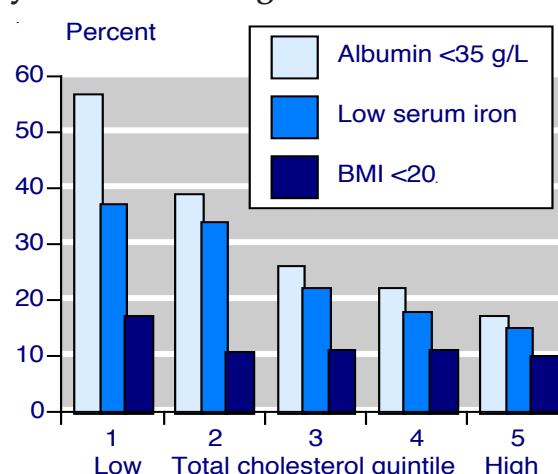
Results

There were 2,486 patients admitted (53% women), with an average age of 78 years, and average total cholesterol of 4.7 mmol/L. Total cholesterol in men aged over 85 years was 12% lower than average than in those aged 65-69. Total cholesterol in women aged over 85 years was 6% lower than average than in those aged 65-69.

Disability indices were higher in those with lower cholesterol, as was the incidence of low serum albumin and iron, and a BMI below 20 (Figure 3). Low cholesterol was independently associated with a diagnosis of infectious disease, low serum albumin and low BMI. After adjustment for these factors, the likelihood of having low serum cholesterol did not increase with age.

Predicting cholesterol reduction [4]

A random sample of people in four medical programmes in the USA recruited 2,800 adults aged 65 years or older, who had a first examination in 1989-1990. Serum cholesterol was measured at visits five and nine years later, and predictors of change sought in a wide range of other demographic and blood measurements.

Results

In the 1,683 men and 1,154 women the average reduction in cholesterol over four years was 0.16 mmol/L. One-third had no change, while 27% of men and 28% of women had reductions of at least 0.5 mmol/L. Larger reductions were seen in people whose starting cholesterol was highest, particularly over 6 mmol/L. Factors associated with greater decline on multivariate analysis were age, male sex, and higher white cell count, serum albumin, and baseline cholesterol.

Cholesterol predicting functional decline [5]

A longitudinal study in a random sample of a Dutch population examined an adult population aged 55 to 85 years with complete data on serum albumin and total cholesterol at baseline. They were asked at baseline and three-year follow

up to perform three simple actions: walk three metres, turn around, and walk three metres back; stand up five times from a kitchen chair with arms folded across their chest; and put on and take off a cardigan. Each was timed, and the times scored according to a simple system.

Results

The mean age of 1,064 participants was 68 years. Low serum albumin (below 43 g/L) was found in 24% of women and 22% of men. Low serum cholesterol (below 5.2 mmol/L) was found in 8% of women and 18% of men. A three year decline in functional performance was associated with low cholesterol in women. In men, functional decline was associated with both low cholesterol and low albumin.

Statin use in older people [6]

The geriatric Ontario Longitudinal database linked several healthcare databases with follow up of mortality over time. It includes 1.4 million residents of Ontario who were alive and 66 years or older in 1998. Information was obtained on medicines prescribed in the year before the cohort began.

The cohort comprised those at high risk of future cardiovascular events, with a history of cardiovascular disease or diabetes. Patients with recent history of cancer were excluded. The final cohort was of 396,000 persons A baseline risk index was created using multiple logistic regression models, and stratified at 25%, 50% and 75% percentiles of death. Low, intermediate and high-risk patients were identified.

Results

Two-thirds of patients in the cohort had cardiovascular disease, 18% diabetes, and the remainder had both conditions. Half were women, and the average age was 75 years. Statins were prescribed in 19%.

Patients prescribed statins were younger, more likely to be men, with a prior heart attack, angina, or invasive procedure, and made more visits to a cardiologist. Patients not prescribed statins were more likely to have diabetes, congestive heart failure, stroke, or live in rural areas.

Figure 4: Cardiovascular risk, mortality, and statin prescription
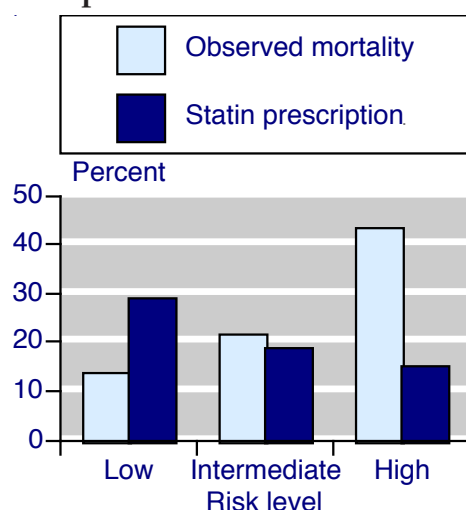
Patients who were older, or at higher baseline risk of dying over the next three years were less likely to have a statin prescribed. Figure 4 show the relationship between observed three-year mortality and statin prescription for the age group 75-80 years. Progressively lower use of statins in patients with higher cardiovascular risk existed across the full spectrum of risk, and across the entire spectrum of age.

Comment

All complicated stuff, and not easy to make into a simple story. But let's try, anyway, at the risk of oversimplifying.

Average cholesterol levels fall with increasing age, and low cholesterol is associated with increased mortality, particularly cancer and causes of death other than cardiovascular, which remains a major cause of death in older people. Cholesterol loss appears to be greater in those with an initially high level. There appears to be a pattern, that low cholesterol is associated with low weight or BMI, or weight loss, poor physical functioning, infections, and other markers of lower health, like low serum albumin and iron.

There are probably several things going on together. Reduced hepatic synthesis, appetite and food intake are expected with increasing age. Superimposed might be differing patterns of comorbidity, and the propensity of some people to age faster than others, for reasons we understand poorly. Fit 90 year olds are not the same as sick 70 year olds.

Perhaps this helps explain the paradox of treating older people with statins. Older people at very high risk probably have additional health problems, possibly of more immediate importance than future cardiovascular events. Prescribing a statin is likely to be low on the list of priorities, particularly where many drugs are already prescribed.

Many prescribers would welcome more and better advice on how or whether to prescribe statins to older people at high risk. In the meantime high cholesterol in older people is a problem that has to be dealt with. We might also consider low cholesterol and albumin levels as markers of poor health. The difficulty is knowing what the cut-off should be for low. It might be 4.0 mmol/L or below in people not on statins, but lower in those on statins or with previous cardiovascular disease.

References:
1   IJ Schatz et al. Cholesterol and all-cause mortality in elderly people from the Honolulu Heart Program: a cohort study. Lancet 2001 358: 351-355.
2   E Casiglia et al. Total cholesterol and mortality in the elderly. Journal of Internal Medicine 2003 254: 353-362.
3   S Volpato et al. The inverse association between age and cholesterol levels among older patients: the role of poor health status. Gerontology 2001 47: 35-45.
4   TA Manolio et al. Predictors of falling cholesterol levels in older adults: the cardiovascular health study. Annals of Epidemiology 2004 14: 325-331.
5   BW Schalk et al. Lower levels of serum albumin and total cholesterol and future decline in functional performance in older persons: the Longitudinal Aging Study Amsterdam. Age and Aging 2004 33: 266-272.
6   DT Ko et al. Lipid-lowering therapy with statins in high-risk elderly patients. JAMA 2004 291: 1864-1870.

WEIGHT LOSS FOR KNEE ARTHRITIS

Knee arthritis is common in older people, and it is as much as anything a mechanical wearing out. We are reasonably sure that exercise early in life is not particularly related to knee arthritis (Bandolier 91), but being overweight may be, because of the extra load excess weight puts on the knee joint, and there is some evidence, from the Framingham study, for instance, that weight loss should reduce arthritic knee symptoms. Until now what has been lacking is a good randomised trial of the effects of weight reduction on patients with knee arthritis. Now we have one [1], we can be more confident that weight reduction is a good thing for people with painful knees.

Randomised trial

The setting was Danish patients who were overweight adults with primary knee osteoarthritis according to standard diagnostic guidelines, with radiological evidence of damage. Overweight was defined as a BMI of over 28 kg/m², and for participation they had to express a clear unequivocal motivation for weight loss and no major health problems.

Included patients were randomised to an eight-week programme of either a low energy diet or a control hypo-energetic high protein diet. The low energy diet (3.4 MJ/day) consisted of a nutrition powder dissolved in water and taken six times a day, with weekly nutritional instruction and behaviour therapy. The control diet (5.0 MJ/day) group received a two-hour baseline instructional session with nutritional advice, and recommended foods and diet plans to provide about 5 MJ/day. Randomisation was stratified according to sex, age and BMI. Patients maintained any OA therapy during the trial.

Measurements of weight and body composition were made at baseline and after eight weeks. Symptoms of OA were measured by the WOMAC questionnaire addressing joint pain, stiffness, and limitations of physical functioning, Lequesne index, and health assessment questionnaire.

Results

After initial randomisation there were several withdrawals (about 10% of initial), and results are reported according to completers, since only they had a final value. At baseline the two groups (40 patients in each) were similar, with 90% women, with an average age of about 63 years, average weight of 97 kg, and BMI of 36.

Weight outcomes

The mean weight loss on the low energy diet was 11.1 kg, and on the control diet it was 4.3 kg. Half those on the low energy diet lost more than 10% of initial weight, compared with none on the control diet, while 93% and 25% lost at least 5% (Figure 1). Most of the weight lost was as fat. The number needed to treat with low energy diet for eight weeks to achieve at least a 10% weight reduction was 2.0 (1.5 to 2.9).

Figure 1: Weight loss on low energy and control diets, percent achieving each level of weight loss
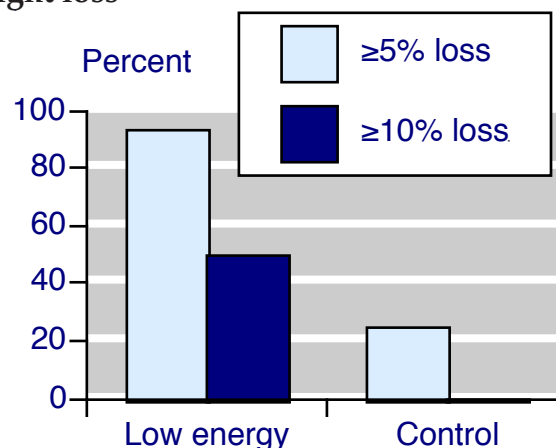

Arthritis outcomes

Patients in both groups had improvements in the WOMAC indices (Figure 2). These were better on the low energy diet than control, significantly so for total score and physical functioning. At least 50% reduction in total WOMAC score occurred more frequently in the low energy group than with the control diet. The number needed to treat with low energy diet for eight weeks to achieve at least a 50% reduction in total WOMAC score was 3.4 (2.1 to 8.8).

The absolute numbers achieving this degree of improvement was not given, but 30% more patients had this degree of improvement with low energy diet for eight weeks than with control diet. There was a general correlation between weight loss and improvement in symptoms. Lequesne index differences just failed to reach statistical significance, and health assessment results were not given. Adverse events were not mentioned.

Comment

There are those who will not like the idea of a rapid weight loss programme, and the relevance of weight loss is well

Figure 2: WOMAC scale outcomes, as percentage decrease from baseline for low energy and control diets
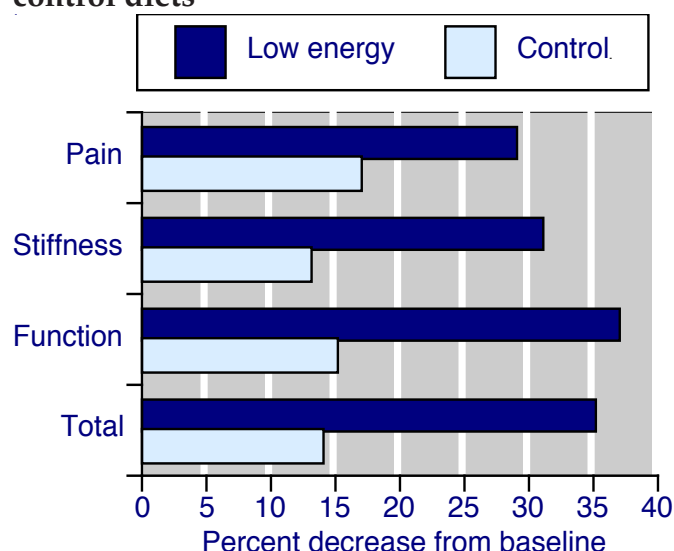
considered in the paper. But for the purposes of determining how reducing overweight contributes to improving symptoms, it is highly relevant. What is impressive is the degree of improvement. NNTs of 2 for significant weight reduction and 3 for significant improvement in arthritis symptoms make one sit up and take notice, despite the relatively small size of the trial and enhanced recruitment.

These results are probably better than most drug treatments could achieve, especially paracetamol (Bandolier 127), and without the known problems associated with NSAIDs, and similar drugs. Weight loss has other benefits as well, on cardiovascular risk, and possibly cancer risk.

The authors describe a typical patient in their clinic: older woman, significantly overweight, trapped in a negative pattern of continual weight gains and pain, accompanied in turn by decreasing activity and functional capacity. Overturning the negative pattern with rapid weight loss looks like a common sense approach worthy of further study, not just in randomised trials for effect, but rather in implementation of what is already known.

Reference:
1   R Christensen et al. Weight loss: the treatment of choice for knee osteoarthritis? A randomized trial. Osteoarthritis and Cartilage 2005 13: 20-27.

Fixed-dose combinations and adherence

Bandolier has previously examined issues about adherence in its pages and on the Internet version, where there is a small library of evidence. Adherence to long-term therapy is low, perhaps not even 50%. A WHO report in 2003 highlighted that simplicity of dosing regimen and adverse effects were therapy-related factors contributing to adherence (make it easier, with fewer adverse events, and people take the tablets).

Ways of improving adherence include combining several therapies in one pill, or using unit-of-use packaging that puts the medications to be used in fixed combination together. A systematic review [1] has assembled what passes for the evidence.

Systematic review

All randomised or quasi-randomised studies meeting various criteria were sought in five major databases, to mid-2003, were used. Criteria were: adult patients, taking more than one oral medication, intervention of combination pill or unit-of-use packaging compared with usual pill containers, and at least one outcome measure relating to adherence, pharmacological goal of medication, or cost.

Results

No quantitative synthesis was likely to be possible from what was a predictably mixed bag of studies. Fifteen tri-

Table 1: Main results of combination therapy systematic review

Improvement trend	Outcome in trials measuring it
12/15	Trends to improve clinical and/or adherence outcomes
7/13	Significant improvement to adherence
4/7	Significant improvement in clinically relevant end-point

als were found, with fixed dose combinations in three and unit-of-use packaging in 12. Settings were:

- management of multiple medications (older people) (5)
- infectious diseases (5)
- blood pressure lowering (3)
- diabetes (1)
- vitamins (1)

Studies had statistical significance or trends towards better adherence or better clinical outcomes more often than they did not (Table 1). Two of three studies examining combination therapy in one pill versus the same medicines separately in tuberculosis or HIV over four months to two years had statistically better adherence, and one tuberculosis study had significantly better clinical outcomes. Of five studies examining unitary packaging in older people with many medications, three performed since 1987 had significant improvements in adherence, but populations were tiny.

Comment

This systematic review is a useful resource for thinking about combination therapies, either as one pill, or as unitary packaging of different pills. It tells us that there is precious little information, that the trials are in a mixed bunch of conditions (they include TB, leprosy, malaria, hypertension) and settings from less to most developed countries. But that is what there is, at least up to mid-2003.

On balance, combinations look useful most of the time, both for adherence and clinical outcomes. That is interesting, especially when attitudes to combination therapies are so mixed. Great for tuberculosis or a magic polypill with five ingredients to banish heart disease. Bad for paracetamol and codeine in older people with pain in the community.

We do know that female sex, older age, and increasing numbers of pills increases the risk of serious adverse drug events. We know that these are common, affecting many thousands of older people. What is daft is that we have so little data, when common sense indicates that the combination of adverse drug events and noncompliance has to be a huge cost in resource and human terms.

Reference:
1   J Connor et al. Do fixed-dose combination pills or unit-of-use packaging improve adherence? A systematic review. Bulletin of the World Health Organisation 2004 82: 935-939.

Hyperbaric oxygen for chronic wounds

Chronic wounds that take a long time to heal, or which recur, are quite common, particularly in older diabetics and people in hospital, and those with multiple health problems. Wound management varies according to the underlying cause of the wound, and there are many options. Despite adequate treatment, some wounds fail to improve, or actually get worse. In some cases, particularly in diabetes, amputation becomes necessary.

Using hyperbaric oxygen to increase oxygenation of tissue and stimulate healing has been proposed, and is used. It is expensive because it involves placing patients in a hyperbaric chamber filled with pure oxygen at pressures above one atmosphere for up to two hours. The procedure is often repeated once or twice a day for up to 30 such sessions. A systematic review of small studies [1] gives a strong hint that there may be real benefits.

Systematic review

Trials had to include a randomised comparison of hyperbaric oxygen therapy compared with sham therapy on air or no therapy for chronic wound healing. Chronic wounds could be related to diabetes, or venous or arterial disease, or pressure. Outcomes were predetermined, as wound size reduction, proportion healed, major amputation (lower or upper limb proximal of hand or foot), minor amputation (distal end of hand or foot), pain, recurrence, or quality of life, together with adverse events. Several electronic registers were used, including a specific database for RCTs in hyperbaric medicine. The last searches were in 2003.
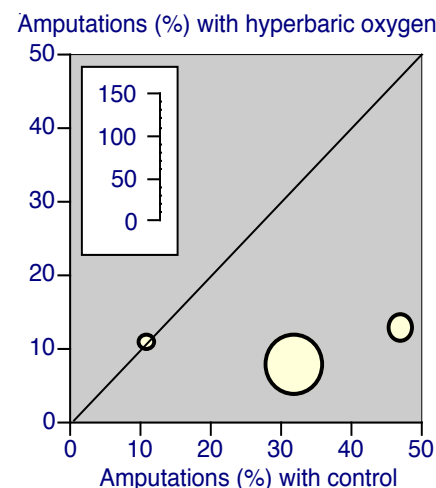
Results

Six randomised trials were found, five in diabetes and one in venous ulcers, with 191 patients, of whom 100 received standard treatment plus hyperbaric oxygen, while the controls received standard wound treatment alone, or with additional sham therapy on air (three trials). Methodological quality was adequate in three, mainly due to issues around blinding and use of sham therapy. Short duration of follow up was also an issue in some trials.

The main results are shown in Table 1. Significant improvements were found for wound size reduction soon after therapy, and for major amputation (Figure 1), where the

Figure 1: Major amputations with hyperbaric oxygen and control

relative risk for major amputation with hyperbaric oxygen therapy was 0.3 (0.1 to 0.7), and the number needed to treat to prevent one major amputation was 4 (2.7 to 12).

Adverse events were noted in some trials. Two cases of pressure trauma to the ear were recorded.

Comment

The use of hyperbaric oxygen for wound healing is a grey area. Some non-randomised studies suggest a moderate benefit, and the small randomised studies appear to confirm that for diabetic ulcers, notwithstanding methodological problems about blinding and follow up. Major amputation is a hard clinical outcome, and it lends weight to the conclusion. There is no more evidence, and additional searching in 2005 found no more randomised trials.

There is obviously scope for bigger and better trials, and for some health economic consideration. It may be expensive for four patients to have 20-30 sessions of hyperbaric oxygen therapy, but the cost and burden of the one major amputation avoided is also likely to be substantial. Even a cursory consideration of the relative costs suggests that balance is likely. It should not be too difficult to determine break points at which effectiveness of treatment is cost effective, or even cost saving. In the meantime this review will provide useful information for purchasers of therapy.

Reference:
1   I Roeckl-Wieddmann et al. Systematic review of hyperbaric oxygen in the management of chronic wounds. British Journal of Surgery 2005 92: 24-32.

Table 1: Main outcomes of randomised trials of hyperbaric oxygen therapy for chronic wounds

Outcome	Studies	Results
Wound size reduction	2	Both studies (one venous ulcer) measuring wound size found significant reduction soon after therapy
Proportion healed	3	In diabetes, 7/24 healed with hyperbaric oxygen vs 1/22 for control, though not significant. No significant improvement in the venous ulcer trial
Major amputation	3	In diabetes, significant reduction in the two largest trials, and overall. NNT 4 (3-12)
Minor amputation	2	In diabetes, 5/24 with hyperbaric oxygen vs 2/24 for control, with no significant difference

Prostate cancer with low PSA

One of the problems with screening tests for cancer is that there is an assumption that if you have a negative test, you don't have cancer. Many people just don't realise that you can have cancer with a negative screening test. For prostate cancer serum PSA levels of 4 μg/L or more are considered to show the possible presence of cancer. An analysis of men in a large randomised study shows that cancer is also found in men with lower levels [1].

Study

The study (Bandolier 114) enrolled men aged 55 years or older with a normal digital rectal examination, and American Urological Association score of 20 or lower (less than severe symptoms of benign prostatic hyperplasia), and a PSA of 3.0 μg/L or lower. Men were given a three-month supply of placebo tablets, and if PSA was confirmed as being 3 μg/L or lower and adherence was within 80% of nominal, they were randomised to finasteride 5 mg/day or placebo.

Men had annual measurements of PSA and digital rectal examinations, and any value above 4 μg/L or abnormal digital rectal examination during the trial prompted a recommendation for prostate biopsy.

This study only included men on placebo who never had a PSA above 4 μg/L or abnormal rectal examination, who never had a biopsy or prostate operation during the study, but who did have a prostate biopsy at the end of the seven-year trial. The presence of prostate cancer on histology, and grading, were related to the PSA value measured at the time.
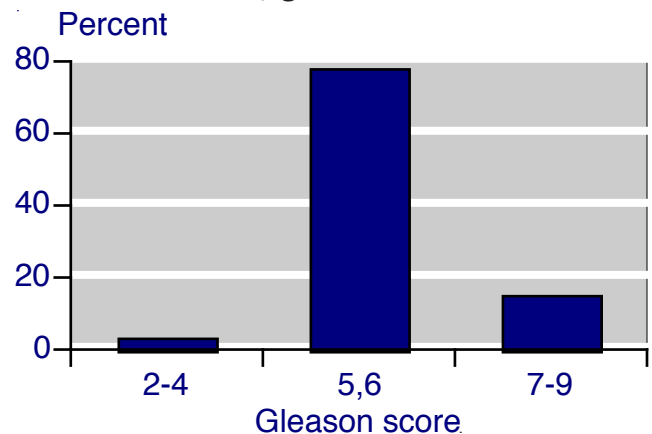
Results

The minimum age was 62 years (range 62-91 years) at end of study, and about a fifth of men were aged over 75 years.

Figure 1: Distribution of serum PSA levels in men with any biopsy detected prostate cancer, and with high-grade (Gleason ≥7) cancer
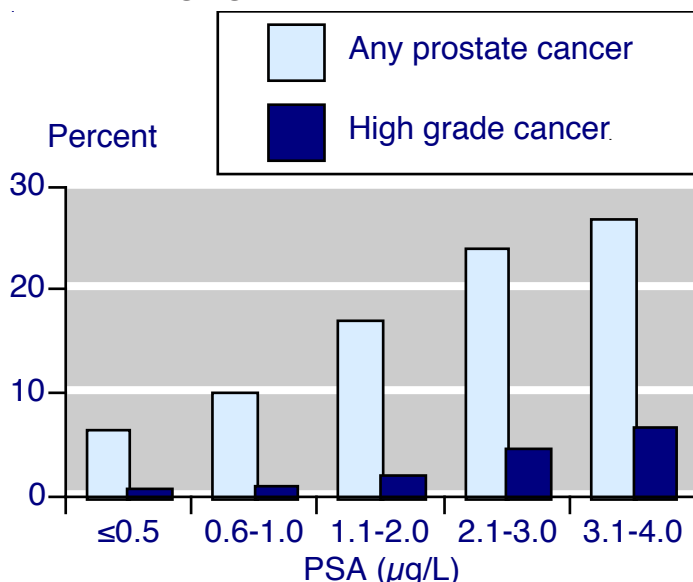
Figure 2: Distribution of Gleason scores among 449 biopsy-detected prostate cancers in men with PSA ≤4 μg/L

Most (94%) were white, and 16% had a family history of prostate cancer, with an affected father, brother, or son. In 2,950 men with PSA values of 4 μg/L or less, 449 (15%) had prostate cancer. The rate was higher (20%) in men with family history than those without (14%).

Men with any prostate cancer were found at all levels of PSA (Figure 1), with increasing prevalence at increasing PSA. Most cancers were low grade, with 77% with Gleason score of 5 or 6, but with 15% with scores of 7 to 9, a grade usually associated with disease progression.

High-grade cancers (defined as a Gleason score of 7 or above) were also found with any level of PSA (Figure 1), rising from about 1% at ≤1 μg/L to 7% at 3-4 μg/L. High-grade cancer was found more commonly among cancers with increasing PSA value.

Comment

Although the risk of finding a cancer on biopsy is directly related to PSA levels below 4 μg/L, there is no PSA value below which a man has no risk of prostate cancer. Moreover, this statement applies not just to any grade of prostate cancer, but even to high grade cancers where disease progression in the absence of treatment is to be expected.

What makes this result so telling is that it was large, was part of a randomised trial in which these men received placebo for seven years, and during which men with elevated PSA above 4 μg/L, abnormal digital rectal examination, or prostate surgery were excluded from this study. At one level, then, the implication is that this is a best-case scenario.

Its importance is that it is a harsh reminder of the failures as opposed to the benefits of screening. Older men with normal PSA values of 4 μg/L or below should still be on the lookout for warning signs, as 1 in 8 will have prostate cancer worth treating despite that normal result.

Reference:
1 IM Thompson et al. Prevalence of prostate cancer among men with a prostate-specific antigen level of ≤4 ng per millilitre. New England Journal of Medicine 2004 350: 2239-2246.

Dry eye incidence

Dry eye syndrome is common in older people, and affects quality of life. Until recently there have been no longitudinal population-based studies that might inform on the likely incidence in a primary care adult population. We now have one [1], and we can say that in people aged 48 to 91 years, 13% will develop dry eye over five years.

Study

Beaver Dam in Wisconsin is the site of a population based eye study that began in 1988. Almost 6,000 adults were then aged 43 to 84 years, and were examined initially and followed up in the years 1988-1990, 1993-1995 and 1998-2000.

Dry eye information was first collected in 1993-1995, when 2,414 people were examined and found not to have dry eye syndrome. At the next examination in 1998-2000 the presence of dry eye, or history of dry eye in the intervening years was established, so that the five-year incidence of dry eye could be established.

Dry eye was determined by a positive response to the question:

> "For the past 3 months or longer, have you had dry eyes?"

For participants needing further prompting, dry eye was described as "foreign-body sensation with itching and burning, sandy feeling, not related to allergy". Considerable additional information relating to demographics and drug history was collected in addition, and used to examine associations with dry eye.

Results

Of the 2,414 participants who did not have dry eye at the baseline in 1993-1995, 56% were women, and the age range was 48 to 91 years. Almost every participant was white. During the five years, 322 adults developed dry eye, a five year incidence of 13% and an annual incidence of 2.7%.

Figure 1: Five year incidence of dry eye in adults, according to age
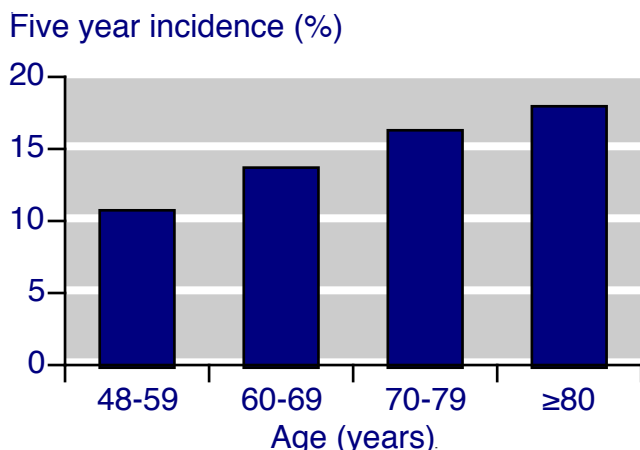
Figure 2: Five year incidence of dry eye in adults, according to self-reported health status
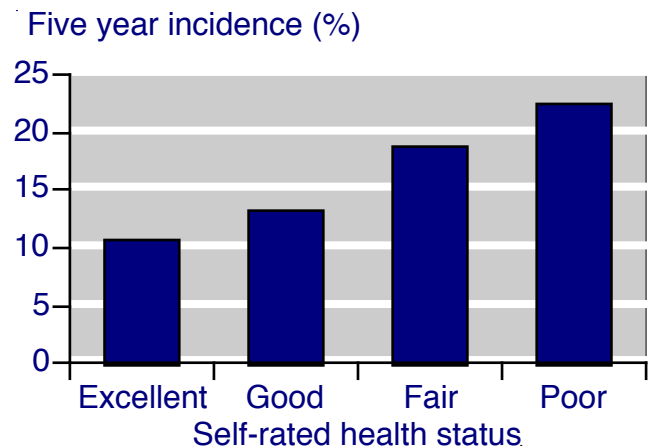
Dry eye incidence increased with age (Figure 1), and was slightly higher in women (15%) than men (12%). Incidence was higher with a history of allergy and antihistamine use, but also with use of diuretics and steroids, and with poorer self-rated health status (Figure 2). It was lower in people using ACE-inhibitors.

Comment

Dry eye is one of those quite common conditions that seems a bit of a mystery. This study is useful in that it provides one solid piece of information from a good study that we can probably trust. The reasons for trusting it include the fact that it was large, conducted over a long period, as part of detailed study of eye disease, and from a defined population rather than a special population, like a clinic or people with a particular disease.

The most useful features are that it gives us a number (almost 3% of older adults will develop dry eye each year), and tells us that it will be more frequent in those with poor health status or who are older (often much the same thing). The association with allergy and antihistamines is probably to be expected, and the relationships of either direction between use of antihistamines, diuretics and ACE inhibitors, while statistically significant, are not of sufficient size to worry about. Bandolier will look for evidence about treating dry eye syndrome.

Reference:

1   SE Moss et al. Incidence of dry eye in an older population. Archives of Ophthalmology 2004 122: 369-373.